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Invited Editorial

Patients' Rights to Laboratory Data: Trinucleotide Repeat Length in Huntington Disease

M.M. Burgess and M.R. Hayden

Office of Medical Bioethics, University of Calgary (M.B.), Calgary, Maurice Young Visiting Research Fellowship, Centre for Applied Ethics (M.B.), and Department of Medical Genetics (M.R.H.), University of British Columbia, Vancouver, Canada

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INTRODUCTION

Huntington disease (HD) is a neuropsychiatric illness which usually manifests in mid-adult life and progresses inexorably, without remission, to death approximately 15–20 years from the time of onset [Hayden, 1981; Harper, 1991]. At the present time there is no treatment to either delay or halt the progression of this illness. Recently, the genetic basis for HD has been defined and this disease is caused by CAG repeat expansion [HDCRG, 1993] which underlies all cases of HD worldwide [Kremer et al., 1994].

Predictive testing for HD has been offered longer than for any other genetic illness. Between 1986 and 1993, predictive testing involved the use of DNA markers closely linked to the mutation for HD, which resulted in a risk change that somebody was either likely or not likely to have inherited the HD gene. The discovery of the mutation underlying HD has now afforded the possibility of determining directly whether someone has or has not inherited the gene for HD. This is ascertained by virtue of assessing whether the proband has CAG expansion in the HD range.

For many patients receiving this information, the question changes from whether they will develop HD to when will it manifest. Even though CAG repeat length is highly sensitive and specific for predicting that someone will develop HD at some time in the future there is limited ability to predict age-of-onset. CAG repeat length in general only accounts for 50% of the variation in age-of-onset [Andrew et al., 1993; Duyao et al., 1993; Snell et al., 1993]. A further complication is the lack of standardization between laboratories often resulting in small differences in estimates of CAG repeat length between laboratories.

Due to the limited predictive abilities of repeat length in most instances, particularly for CAG repeat sizes in the HD gene between 38 and 50, many American and Canadian centers have a policy of not disclosing CAG repeat length as part of the results [Duyao et al., 1993; Benjamin et al., 1994; Huntington Disease Study Group, personal communication]. However, as persons at risk for HD become aware of how the test is conducted (i.e., that numbers of CAG repeats are measured), some have begun to request the actual number of CAG repeats detected. Some centers have accepted the patient's right to know this information, and do disclose it. For example, some European centers, such as those in Sweden, routinely disclose repeat length. The appropriateness of this practice is controversial, in part because there are anecdotal reports of relatives comparing repeat lengths, inaccurately reporting lengths, and misinterpreting the significance of differences in repeat length.

The strength and vehemence with which these positions are asserted suggest that they are held as moral positions about appropriate clinical practice (i.e., disclosing or not disclosing). What is the moral controversy behind the issue of disclosure of repeat length to persons who have CAG repeat length in the affected range?

PRINCIPLE-BASED MORAL ANALYSIS

As a first step in this ethical analysis, consider 3 alternative policies, and the ethical principles that each of them promote. The alternatives are as follows:

1. Never disclose CAG repeat length.
2. Always disclose CAG repeat length.
3. Sometimes disclose CAG repeat length.

The "never disclose" position is a strongly paternalistic position, placing the greatest ethical weight on the avoidance of any harm to the patients. "First, do no harm," or nonmaleficence is a frequently cited principle of medicine, as well as of other health care disciplines [Beauchamp and Childress, 1989]. It is an important principle, particularly when the methods of medicine

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Dr. M.M. Burgess's current address is Chair of Bioethics, Centre for Applied Ethics, University of British Columbia, 6356 Agricultural Road, Vancouver, BC, Canada V6T 1Z2. Address reprint requests there.

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have often been powerful or invasive, capable of much damage, and to be used only when the expected benefit exceeds that of the harm. The second moral principle, promoting benefit or beneficence, is another central principle to the health professions [Beauchamp and Childress, 1994]. There is a strong professional responsibility to avoid any professional service that risks harm unless there is a justifying benefit. When repeat length is of no predictive value, it seems that there is no benefit to be derived from disclosure of repeat length. However, disclosure does carry some risks. The individual may misinterpret CAG repeat length to be indicative of severity or age-of-onset, particularly when compared to other relatives or other persons' repeat length. Relatives, employers, and others may also believe that the CAG repeat length accurately predicts onset. Since there is some risk of harm, and no likely benefit, it seems professionally responsible to withhold information concerning CAG repeat length. Informing participants that this approach is being undertaken does not reduce the paternalism nor does it constitute consent in the absence of any other options.

One further characteristic of the nature of the information concerning CAG repeat lengths may support the nondisclosure option. Since repeat length in most instances has no implications for prediction of onset or treatment, it is not obvious that its disclosure enhances autonomy. If the basis for a "right to know" is the promotion of autonomous choices, then it may be that the right does not apply to information concerning CAG repeat lengths. Much depends on whether enhancement of well-informed decisions or more general self-knowledge is the goal of enhancing autonomy.

The "always disclose" position promotes autonomy in what may be described as an antipaternalist stance. The recent emphasis on autonomy has developed in part as a corrective to overdependence on professional responsibility as the entire ethic in health care [Katz, 1984; Beauchamp and Childress, 1989; Faden and Beauchamp, 1986]. Respect for autonomy has resulted in the promotion of informed consent as a central doctrine in health care. Patients consider all the relevant information and make voluntary choices with the guidance of health professionals. Since it is difficult to know what each patient might consider relevant, standards of disclosure have tended toward complete disclosure or disclosure of whatever information is relevant to each patient as an individual. The strong notion of respect for autonomy effectively established the patients' right to information about themselves, which could facilitate decisions about their health, and as a counter to paternalism in health care. This trend is strongly reflected in recent ethics literature about access to, and the right to choose not to receive, genetic information [Knoppers and Laberge, 1989; Knoppers, 1991].

The "always disclose" position is probably most strongly defended from an antipaternalism stance constituting one's right to such information. Based on this approach, deliberation about whether there is adequate benefit to justify the potential harms of disclosure is unnecessary. Harms of the simple provision of information are likely to be of minor magnitude or result from voluntary reactions of the recipients and therefore should not limit access. Access to information about oneself and treatment according to one's wishes are essential to the notion of autonomy. Legal deliberations also support broad disclosure and patient-centered determination of the relevance of information is recommended unless the patient is unable to provide informed consent [Canterbury, 1972; Halushka, 1965; Hopp, 1980; Reibl, 1980; Weiss, 1989]. Full disclosure ought to encourage patients to become more involved and accept responsibility for their health care. From this stance in support of patient autonomy, the "always disclose" position seems to be the most defensible. Legal deliberations also support broad disclosure and patient-centered determination of the relevance of information unless the patient is unable to provide informed consent [Canterbury, 1972; Halushka, 1965; Hopp, 1980; Reible, 1980; Weiss, 1989].

Alternatively, there might be another basis for claiming a right to this information that does not depend on it influencing decision making. An individual may simply feel that the CAG repeat length used to predict the risk of developing HD is personal and reflects something intimate about the person's genetic makeup which may also be transmitted to their offspring. Although the nondisclosure position does not deprive one of information relevant to any particular decision, it may represent data that one would value as personal information. In this view, promotion of autonomy may also include allowing persons to develop their own personal self-concept in a manner enhanced by disclosure, even though disclosure may not directly enhance decision-making capacity.

The "sometimes disclose" position recognizes that there is some wisdom in using professional judgment to determine when harms of disclosure outweigh benefits, yet that it is paternalistic to make such judgments in the case of information unless there are good grounds to be concerned about harms [Knoppers and Laberge, 1989; DeGrazia, 1991]. Disclosure of CAG repeat length might be considered only when patients request it and there are no good grounds to believe that harms will ensue. But this places persons who may not know that they may request this information at a disadvantage. A fair policy might be to inform patients that CAG length is measured, to provide information on the limitations of CAG repeat length in predicting onset, and to provide disclosure of CAG repeat lengths if requested except in unusual circumstances where harm is expected. One potential harm may be that persons with knowledge of their CAG repeat length may not be suitable for therapeutic trials as this could be viewed as a potential bias both for investigators accessing the efficiency of a particular medication and for persons receiving this medication.

Determining which approach is most ethically defensible requires further information about the harms, benefits, and the effect on autonomy of disclosure of repeat length in HD. Specifically, the effects of disclosure of CAG repeat lengths on patients must be studied. The effects are likely to be difficult to measure because of highly variable effects on self-esteem, self-identity, con-

fidence, social activity, and the reactions of others. Presumably, the most probable harm of greatest magnitude is misinterpretation leading to emotional harm or misinformed decisions. Professional responsibility for these harms might be better fulfilled if misinterpretation could be avoided through improved counseling and identification of circumstances that might combine to lead to harms. In an effort to assess the harms and benefits of providing repeat length as part of predictive testing, the collaborators have devised a study which is now underway, to assess these effects. Significantly, potential harms due to laboratory differences in protocols could be minimized by quality control measures and the use of appropriate standardized size markers.

A CONCEPTUAL CLARIFICATION

However, the tools of contemporary ethical analysis have not been exhausted. Furthermore, the ethical analysis to this point has not captured satisfactorily the ethical concerns expressed by health care professionals debating appropriate policy and practice for disclosure of repeat length at our center. Feminist philosophers and some ethicists suggest a more contextual approach to ethics based on caring relationships among involved persons [Baier, 1986; Hoffmaster, 1992; Sherwin, 1992; Toulmin, 1981; Winkler, 1993]. The insights derived from these analyses suggest that the principle-based approaches may inadequately encompass the full range of ethical concerns [Hoffmaster, 1992; Nedelsky, 1993; Winkler, 1993].

These analyses often combine narrative accounts which include very specific details to assure that the moral analysis is sensitive to the particular circumstances. The following section identifies previously unrecognized features of an ethical problem through careful analysis of clinicians' reflections on a single participant's experience. These insights support the "sometimes disclose" option.

During discussions of the risks and benefits of disclosure of repeat length, the members of the Canadian Collaborative Study on Predictive Testing for HD have articulated concerns beyond that of autonomy, beneficence, and nonmaleficence. Early discussions concerning the policy at different centers led to the discovery that practices varied between centers, with some reports of relatives in different cities being given different types of results. In our center, the challenge to our policy of nondisclosure of CAG repeat length came from a participant for whom repeat length had become particularly significant. She insisted that she "had a right to information about (her) medical health." She stated that "what we as individuals do with this information is our responsibility and ours alone. The only legitimate role of the predictive testing team is to provide the information and to make every effort to ensure that the information is properly understood. Your role is to put in place appropriate counseling to ensure to the best of your ability that the information is properly understood." The discussion progressed from defending the paternalist policy to whether nondisclosure was contributing to a process and shaping relationships that were nonbeneficial and perhaps even harmful for this patient. It was suggested that once the information was disclosed, it would be of far less significance, and supportive relationships with the person could be maintained.

The clinical team providing results of predictive testing did not change their view that CAG repeat length did not provide accurate information about age-of-onset. Rather, disclosure of this information was a means of supporting this particular relationship. This experience led to a review of the appropriateness of the entire policy of uniform nondisclosure. In this particular case, it seemed that the CAG repeat length information had personal significance, even though the individual understood its lack of clinical significance. This was direct experience for the health professionals of how the information about repeat lengths could be meaningful to an individual, quite apart from its failure to provide accurate information about age-of-onset or natural history of the disease. Further, the health professionals could understand how nondisclosure might appear to be disrespectful when these data were clearly available in the laboratory, and that the policy of nondisclosure contributed to the person's lack of trust in the process. Reevaluating the terms of nondisclosure relative to the harms of disclosure, the clinicians began to be concerned with a research design that randomized patients to disclosure or nondisclosure of CAG repeat length. They expressed this as a lack of comfort with nondisclosure to any patient who wishes to have this information. Once they had accepted that the policy could be one of considering disclosure of repeat length, it was very difficult to return to the belief that they had a professional duty to withhold this information when a patient requested it.

The group gained insight into how the information about repeat length can become personally significant even though it is not indicative of age-of-onset. This experience led to a reevaluation of the harm and benefits of disclosure. Once this disclosure was seen to reflect trust and respect for one participant, it was very difficult to return to the belief that there was a professional duty to withhold this information when participants wanted it. Withholding the data was now recognized to be a harm for this person in that it failed to reflect trust and respect of her request.

DO PATIENTS HAVE A RIGHT TO ALL LABORATORY DATA?

What is the relevance of this experience to other diseases caused by triplet repeat expansion, or laboratory data in general? The experience has taught us that laboratory data that are not informative for clinical purposes may still be desired by patients. Health care professionals may misinterpret the patients' request for these data as evidence of their misunderstanding its significance. However, patients may experience the denial of access to this information as distrust, and the loss of trust in these relationships is a definite harm. This does not suggest that all laboratory data must be made available to patients. Rather, requests for laboratory data should be evaluated to determine whether the risks of disclosure (i.e., misunderstanding or possible uses or misuses) are actually greater than the harm of

loss of trust and disrespect resulting from refusal to provide this information.

Three points are relevant for consideration. Firstly, the policy of seeking and fulfilling participants' wishes enables individuals to choose to have or not have this information. Routine disclosure would not provide the same range of personal choice and opportunity to avoid risks. Whenever disclosure of laboratory data of questionable significance is contemplated, this more cautious approach is likely to balance the risks of disclosure with trusting and respectful relationships.

Secondly, counseling is already accepted as part of the care for participants in predictive testing programs and establishes relationships based on trust of participants as competent to receive and manage genetic information. The ascertainment of the repeat length does not incur further expenses, and the counseling concerning repeat lengths can be integrated into current genetic counseling practices. However, counseling including specific repeat sizes could take longer and therefore incur additional expense. For many persons, however, not providing such information may not be experienced as a loss of trust. Clearly each situation must be individually assessed.

Third, the probability and magnitude of harm, or harm to third parties, cannot be evaluated in the abstract. These assessments are influenced not only by the nature of the data, but also by the ranges of responses in the at-risk population, and their social system (such as family, employers, insurers, health care professionals, and institutions). Potential harms of disclosure require assessment for the specific type of data within a particular population located in its social context. The ongoing study of the effects of disclosure compared to nondisclosure of CAG repeat length may provide further information and shape this policy in the future.

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